ISSN: 2643-4539

Heller et al. Int J Neurodegener Dis 2019, 2:008
DOI: 10.23937/2643-4539/1710008
Volume 2 | Issue 1
Open Access

International Journal of
Neurodegenerative Disorders

RESEARCH ARTICLE

Parkinson's Disease, Diabetes, Functional Decline and Cognitive Impairment: A Comparative Study of Elderly Mexican Americans and Non-Hispanic Whites

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Abstract

Objective: Assess moderating effects of functional decline on the associations between late-life cognitive impairment (CI_{mp}) and diabetes and Parkinson's disease (PD); including controls for Mexican-American ethnicity, education, life satisfaction, age, and sex.

Methods: In-home interviews with 1,252 elderly Mexican-American (N = 799) and non-Hispanic white (N = 353) residents of El Paso County, Texas. CI_{mp} measured by MMSE, CLOXI and CLOXII; functional impairment (ADL_{imp}) as impairment in 1-10 activities of daily living. Our hypothesis is that ethnicity will effect variance of diabetes, hence cognitive decline.

Results: Logistic regression analyses--After controlling for effects of all above-cited variables, PD remains significantly associated with the three measures of CI_{mp}, including impairment in executive control function. Controlling for ADL_{imp} does not extinguish the significant association between diabetes and CI_{mp} on any of the three measures. However, no significant degree of association between diabetes and CI_{mp} remains after other control variables (including Mexican-American ethnicity) have been added to the equation.

Conclusions: 1) PD findings are statistically and clinically meaningful. After controlling for all other variables, the OR for respondents diagnosed with PD (compared to their non-diagnosed counterparts) is 1.42 for MMSE impairment (95% CI1.10-15.53); 4.12 for CLOXI impairment (95% CI 1.07-15.85); and 10.51 for CLOXII impairment (95% CI 2.55-43.41). 2) The connection between diabetes and CI_{mp} is problematic; our findings suggest that many of the earlier-reported research findings linking diabetes with CI_{mp} may be an artifact of other intervening phenomena such as regional and ethnic differentials in prevalence rates for diabetes. 3) The relationship between CI_{mp} and ADL_{imp} is strong and clinically meaningful; for each unit increase in ADL_{imp} there is a corresponding 1.33 increase in odds for MMSE impairment (95% CI 1.15-1.55). For impairment on CLOX1 and CLOX2 the ORs are 1.22 (95% CI 1.05-1.42) and 1.21 (95% CI 1.03-1.42). 4) When coupled with other research findings, Mexican-American ethnicity may itself represent a risk factor for CI_{mp}. After controlling for effects all other variables, El Paso's elderly Mexican Americans possess odds 2.46 times greater than those for NHWs in MMSE impairment (95% CI 1.42-4.25); 1.53 (95% CI 1.06-2.20) times greater for impairment in executive control function (CLOXI); and 2.35 times greater for impairment in ability to perform a simple copying task (1.35-4.09). 5) Our findings point to the importance of utilizing a number of different screening devices for assessment of cognitive function in order to increase the likelihood that results can be taken as valid, dependable, and clinically meaningful for elderly individuals a Hispanic ethnicity.

Keywords

Cognitive impairment, Diabetes, Parkinson's disease, Hispanic

Introduction

A number of studies have linked Parkinson's disease (PD) [1-4] and diabetes [5-11] to cognitive impairment (CI_{mp}). CI_{mp} has also been connected linearly [12-16] and/or reciprocally [17] to functional decline. Howev-

Citation: Heller PL, Briones DF, Wilcox JA, de la Rosa JM (2019) Parkinson's Disease, Diabetes, Functional Decline and Cognitive Impairment: A Comparative Study of Elderly Mexican Americans and Non-Hispanic Whites. Int J Neurodegener Dis 2:008. doi.org/10.23937/2643-4539/1710008

Accepted: July 09, 2019; **Published:** July 11, 2019

er, linkages between PD, diabetes and CI_{mp} have either not been universally reported [13,18,19] or have been described as relatively complex [2,20-22]. Diabetes is known to be more common among Hispanic populations and we conducted this study to examine the interactions between ethnicity, and the occurrence of diabetes, Parkinsonism and cognitive decline in a community sample [23].

We report logistic regression analyses findings from a community sample of elderly Mexican Americans and non-Hispanic whites demonstrating that degrees of associations between diabetes and PD with CI_{mp} persist after controlling for effects of functional decline. However, after adding effects of a number of control variables (including ethnicity) to the equation, association between diabetes and CI_{mp} is no longer significant. We suggest that these findings may well be an artifact of the high prevalence of diabetes among elderly Mexican Americans.

Methods

Hypothesis: That ethnicity and diabetic disease will vary in a manner that allows prediction and assessment of cognitive decline and Parkinson's Disease, given the known variable of ethnic differences between Hispanic and non-Hispanic populations.

Survey participants

The purpose of this study was to assess the association between ethnicity, diabetes and Parkinson's disease related cognitive decline in an elderly sample in Hispanic and non-Hispanic individuals.

We interviewed a stratified random sample of 1,152 non-institutionalized elderly (65 years and older) residents of El Paso County, Texas, during 2000-2001. This sample represents 84 percent of respondents originally contacted for interview. The survey instrument was translated into Spanish through cross-translation. In-home interviews were conducted in Spanish or English, depending on respondents' preference. Twenty-four census tracts were randomly selected from 94 census tracts specified in the 1990 census after stratification for median income and ethnic composition. Specifically, eight census tracts were randomly selected from the lower, middle, and upper-middle income categories. Each of these 24 census tracts was screened through telephone interviews to identify households containing one or more members 65 years of age or older. Screening interviews also provided demographic information including respondent's age, gender, and ethnicity. Independent random sampling procedures were then established for Hispanics and non-Hispanic Whites. These procedures ensure virtually equal representation, within each of the three census-tract income categories, of women and men, and age cohorts 65-74 and 74-and-older. Mean and median ages for the entire sample are 74.9 and 74.0. Fifty percent of the sample is female.

Assessment of cognitive impairment

CI_{mp} has been ascertained with three measures: A global assessment of cognitive function through the MMSE [24]; an assessment of executive control function through CLOXI [25]; and a simple CLOXII copying task that is somewhat independent of executive skills [25]. Executive control functions measured by CLOXI are cybernetic processes that control one's ability to initiate, sequence, and monitor complex goal-directed activities [26]. CLOXII measures constructional praxis [25]. CLOXI and CLOXII have been validated in elderly Mexican-American and non-Hispanic White populations [27]. CLOX has also been shown to improve on the sensitivity of the MMSE to various sociocultural influences [28,29]. Impaired cognitive function is operationally defined as a score less than 25 (MMSE), less than 10 (CLOXI), and less than 12 (CLOXII). These cutoff criteria are based on previously reported performance results from cognitively impaired populations [25].

Assessment of specific diseases

Specific diseases are assessed by asking whether a doctor had told respondent that he/she had a heart attack (coronary/myocardial infarction/coronary thrombosis), high blood pressure, diabetes (sugar in urine/high blood sugar), stroke, broken hip, cancer, arthritis (rheumatism), or Parkinson's disease. Bivariate cross-tabulation findings indicate that, of these 8 diseases, only diabetes and PD significantly associate with all three measures of cognitive function; only diabetes and PD are included in multivariate analyses. Almost 25% (N = 284) of our sample have been formally diagnosed with diabetes, as opposed to less than 2% with PD (N = 17). Percentages for diabetes among Mexican Americans and NHWs are 30.5 versus 11.7, a significant difference clinically as well as statistically. Percentage differences in PD for the two ethnic groupings are not statistically significant (Mexican Americans = 1.4%; NHWs = 1.7%). As can be seen in the 95% confidence interval summaries for PD (Table 1) the small number of formally diagnosed PD respondents renders odds ratio (OR) interpretation problematic. On the other hand, statistically significant results for small samples are highly salient. The degree of severity of Parkinson's disease was considered to be mild to moderate in this sample. Patients with the diagnosis of Lewy Body dementia were excluded in order to maintain a minimum number of confounding variables.

Assessment of functional decline

Functional decline is defined as impairment in activities of daily living (ADL_{imp}). ADL_{imp} is measured by asking respondents if they can perform 10 activities without help (telephoning, drive car/travel alone on a bus or taxi, go grocery shopping, prepare meals, do light housework, take medicine, handle money, do heavy work around the house, walk up-down stairs, walk half-

Table 1: Logistic regression analysis predicting impaired cognitive function[a] for parkinson's disease and diabetes mellitus (N = 1152).

Subtable 1A MMSE	**Block 1**				**Block 2**				**Block 3**			
Variable	B	OR		95% CI	B	OR		95% CI	B	OR		95% CI
Constant	-1.38				-1.53				-0.52			
Parkinson's	1.71**	5.53	1.77	17.23	1.43*	4.17	1.28	13.65	1.42*	4.14	1.10	15.53
Diabetes Mellitus	0.67***	1.95	1.42	2.68	0.58***	1.79	1.30	2.48	0.26	1.30	0.90	1.87
ADL (Impaired)[b]					0.40***	1.50	1.31	1.72	0.29***	1.33	1.15	1.55
Ethnicity (Mexican-American)									0.90***	2.46	1.42	4.25
Education (HS Graduate)									-1.55***	0.21	0.14	0.33
Life Satisfaction									-0.05**	0.95	0.92	0.98
Age (75+)									0.74***	2.09	1.50	2.92
Sex (Female)									-0.09	0.91	0.66	1.26
Nagelkerke R^2	0.04				0.09				0.30			
Subtable 1B CLOX1	**Block 1**				**Block 2**				**Block 3**			
Variable	B	OR		95% CI	B	OR		95% CI	B	OR		95% CI
Constant	-0.72				-0.80				-1.14			
Parkinson's	1.84**	6.31	1.72	23.14	1.62*	5.07	1.35	19.03	1.42*	4.12	1.07	15.85
Diabetes Mellitus	0.38**	1.47	1.09	1.97	0.34*	1.40	1.04	1.89	0.23	1.26	0.92	1.73
ADL (Impaired)[b]					0.29***	1.34	1.15	1.55	0.20**	1.22	1.05	1.42
Ethnicity (Mexican-American)									0.42*	1.53	1.06	2.20
Education (HS Graduate)									-0.55***	0.58	0.42	0.80
Life Satisfaction									-0.00	0.99	0.97	1.03
Age (75+)									0.71***	2.03	1.54	2.66
Sex (Female)									0.05	1.05	0.80	1.37
Nagelkerke R^2	0.02				0.04				0.12			
Subtable 1C CLOX2	**Block 1**				**Block 2**				**Block 3**			
Variable	B	OR		95% CI	B	OR		95% CI	B	OR		95% CI
Constant	-1.72				-1.81				-134			
Parkinson's	2.68***	14.74	3.87	54.76	2.44***	11.10	2.96	44.07	2.35***	10.51	2.55	43.41
Diabetes Mellitus	0.62***	1.87	1.31	2.66	0.57**	1.77	1.24	2.53	0.28	1.32	0.90	1.94
ADL (Impaired)[b]					0.29***	1.34	1.15	1.55	0.19*	1.21	1.03	1.42
Ethnicity (Mexican-American)									0.86**	2.35	1.35	4.09
Education (HS Graduate)									-0.97***	0.38	0.24	0.60
Life Satisfaction									-0.04*	0.96	0.93	0.99
Age (75+)									0.54**	1.72	1.21	2.45
Sex (Female)									0.38*	1.46	1.03	2.07
Nagelkerke R^2	0.05				0.07				0.19			

[a]Based on a total MMSE score less than 25 (out of 30); total CLOX1 score less than 10 (out of 15); total CLOX2 score less than 12 (out of 15); [b]Impairment in zero through 10 activities of daily living; *p < 0.05; **p < 0.01; ***p < 0.001 (1-tailed).

mile).

Assessment of control variables

Control variables include ethnicity, life satisfaction, education, age and sex. Ethnicity is defined through respondent's self-selection and childhood and adolescent developmental history. This procedure has yielded samples of 799 elderly Mexican Americans and 353 NHWs. Life satisfaction is measured with a 12-item scale [30] containing the response format, "Disagree", "?" "Agree". Total scale scores can range 12-36. Chronbach's *alpha* for this scale is 0.77 among the El Paso County sample. Life Satisfaction is included as a control variable because quality of life and/or life satisfaction appear to be associated with diabetes [31] and PD [2,32]. This variable is also linked with functional capacity [31] and cognitive function [32].

Educational attainment is included because of its powerful influence on time of onset for cognitive impairment [33]; and is measured as years of formal education, including ordinal categories for "high-school graduate", college graduate", and "at least some post-college education". Thirty-five percent of the Mexican-American sample possesses at least a high school degree, thus providing a meaningful comparison between ethnic groupings. Age (65-74 versus 75 and older) and sex (male = 0; female = 1) are also included as control variables.

Analysis

Logistic regression analyses are conducted for each of the three cognitive function measures. These analyses provide tests of significance and odds ratios for each independent variable (IV) on CI_{mp} after controlling for effects of all other IVs in the statistical equation. Analyses are conducted in three blocks. PD and diabetes are entered in Block 1. ADL_{imp} is added to the equation in Block 2; and effects of all 8 independent variables are assessed in Block 3.

Results

Parkinson's, diabetes and cognitive impairment

Logistic regression results are summarized in Table 1. Shown for MMSE, CLOXI and CLOXII are variable-by-variable effects on CI_{mp} after controlling for effects of all other variables in the equation. Blocks 1 in Subtable 1A, Subtable 1B, and Subtable 1C indicate that diabetes and PD are significantly, and somewhat independently, associated with CI_{mp} on all three measures. The OR of 1.95 for diabetes in Subtable 1A (after controlling for effects of PD) indicates that respondents with diabetes possess odds for MMSE-impairment 1.95 times those of their non-diabetic counterparts. The corresponding OR for respondents diagnosed with PD is 6.31. Similar outcomes are found in Subtable 1B, and Subtable 1C when CI_{mp} is measured with CLOXI and CLOXII. The odds for executive function impairment (CLOXI) among those enduring PD are 6.31 times those for non-sufferers. The corresponding OR for elderly respondents diagnosed for diabetes is 1.47. Both diseases appear to impair cognitive performance related to the straightforward copying task required in CLOXII. Relevant ORs for PD and diabetes in Subtable 1C are 14.74 and 1.87.

Moderating and direct effects of functional decline on cognitive impairment

ADL_{imp} is added to the equation in Blocks 2 of Subtable 1A, Subtable 1B, and Subtable 1C. In none of the three measures of cognitive function does ADL_{imp} render effects of PD and diabetes on CI_{mp} statistically non-significant. ORs for PD and diabetes relating to MMSE impairment are 4.17 and 1.79; for CLOXI impairment (executive control function), 5.07 and 1.40; and for CLOXII impairment, 11.10 and 1.77. All three variables (PD, Diabetes, and ADL_{imp}) independently affect CI_{mp} whether this construct is operationally defined by MMSE, CLOXI, or CLOXII. The OR depicted for ADL_{imp} in Block 2 of Subtable 1A indicates that each unit increase in ADL_{imp} elicits a 1.50 unit increase in odds for MMSE impairment; corresponding 1.34 unit increases in ORs (Blocks 2, Subtable 1B, and Subtable 1C) are found for CLOXI and CLOXII impairment.

Control variables and cognitive impairment

A clear separation occurs in the relative explanatory powers of PD and diabetes on CI_{mp} when all IVs are represented in the statistical equation (Blocks 3, Subtable 1A, Subtable 1B, and Subtable 1C). Remarkably, PD, despite the small numerical size of this diagnosed sample, continues to significantly associate with CI_{mp} after controlling for effects of Mexican-American ethnicity, education, life satisfaction, age, and sex. Effects of PD on CI_{mp} remain salient whether this phenomenon is defined globally through MMSE (OR = 4.14; Block 3, Subtable 1A), as executive control with CLOX1 (OR = 4.12; Block 3, Subtable 1B), or through CLOXII's simple copying task (OR = 10.51; Block 3, Subtable 1C). Diabetes, however, no longer significantly associates with CI_{mp} on any of the three measures.

Like PD, ADL_{imp} continues to significantly associate with CI_{mp} after effects of all other IVs are removed from this variable. With respect to MMSE impairment (Block 3, Subtable 1A) the OR for ADL_{imp} is 1.33; for CLOX1 impairment (Block 3, Subtable 1B), 1.22; and for CLOX2 impairment (Block 3, Subtable 1C), 1.21. Nevertheless, findings reported in Blocks 3 of the three sub-tables in Table 1 clearly indicate that ADL_{imp} by itself produces little consequence on either the PD-CI_{mp} or the diabetes-CI_{mp} relationship.

Finally, it should be noted parenthetically that, in addition to PD and ADL_{imp}, Mexican-American ethnicity and advanced age independently contribute to CI_{mp} on all three measures (Blocks 3 or Subtable 1A, Subtable 1B, and Subtable 1C). Conversely, education appears to prolong the onset of CI_{mp}, as measured by MMSE and CLOX. Life satisfaction, negatively associates with CI_{mp} when this variable is assessed globally (MMSE) or through a simple copying task (CLOXII). However, after controlling for effects of other variables in the equation, life satisfaction does not significantly contribute to impairment of executive function (CLOXII, Block 3, Subtable 1B).

Discussion

Parkinson's and cognitive impairment

Our findings indicate in a stratified, random sample of 1,152 Mexican-American and NHW elderly residents of El Paso County, Texas, that PD is significantly associated with CI_{mp} on three disparate measures of this phenomenon. Despite the small number of respondents

formally diagnosed with PD, its association with CI_{mp} remains significant after the powerful effects of education, age, ADL_{imp}, and Mexican-American ethnicity are removed from the statistical equation (Blocks 3, Subtable 1A, Subtable 1B, and Subtable 1C). The ORs for PD sufferers are 4.14 on the MMSE, 4.12 on CLOXII, and 10.51 on CLOXII. It should be noted that effects of tremor on ability to draw do not contribute to cognitive function scoring on either of these Clock drawing tests [25], or drawings associated with the MMSE [24]. Thus, along with above cited research findings, we suggest that our PD findings are clinically meaningful. We suggest that medical professionals involved with the treatment of PD patients be aware of the possibility of a PD-CI_{mp} connection during ongoing treatment.

Diabetes and cognitive impairment

The connection between diabetes and CI_{mp} is problematic. Results presented in Blocks 2 of Subtable 1A, Subtable 1B, and Subtable 1C indicate that after adjusting for PD and ADL_{imp}, and prior to controlling for effects of Mexican-American ethnicity, educational attainment, life satisfaction, advanced age, and sex, diabetes somewhat independently associates with cognitive impairment on all three measures. However, the inclusion of all IVs in Block 3 of each sub-table renders diabetes a non-significant predictor of CI_{mp}, regardless of how this phenomenon is measured. It is possible that the significant findings for diabetes depicted in Blocks 1 & 2 may be an artifact of the relatively high prevalence of diabetes (30.5%) for El Paso's elderly Mexican-American population (compared to an 11.7% prevalence rate for NHWs). In order to test this idea we cross tabulated diabetes and CI_{mp}, controlling for Mexican-American-NHW ethnicity. No significant degree of association was found between diabetes and CI_{mp} among NHWs on either of the three measures. Diabetes did associate with MMSE impairment ($p < 0.05$) among elderly Mexican Americans, but no significant findings were found for CLOXI or CLOXII impairment. The MMSE findings are in line with those reported for the Hispanic Epidemiologic Study of the Elderly (H-EPESE) [11]; however non-significant findings for diabetes and CI_{mp} have been reported in the New Mexico Elder Health Study [19] in which cognitive function was also measured with the MMSE. It is thus possible that many of the earlier-reported research findings that link diabetes with CI_{mp} may actually be an artifact of other intervening phenomena such as regional and ethnic differentials in prevalence rates for diabetes. Thus, it is yet to be determined whether the relationship between diabetes and CI_{mp} is clinically relevant.

Functional decline and cognitive impairment

No such doubts exist about the relationship between cognitive and functional and impairments. Results reported in Table 1 (Blocks 3, Subtable 1A, Subtable 1B, and Subtable 1C) indicate that for each unit increase in ADL_{imp} there is a corresponding 1.33 unit increase in odds for MMSE impairment. Corresponding ADL findings for CLOXI and CLOX2 are 1.22 and 1.21. The significant nature of these associations is compatible with those reported in a large number of other studies, including the above-cited. The only debate in this area appears to be causal direction. Is ADL_{imp} a derivative of CI_{mp}, or is this relationship more reciprocal in nature? [17] Whatever the causal connection, these statistically significant findings are clinically relevant to medical professionals who deal with patients undergoing cognitive decline.

Mexican-American ethnicity as risk factor for cognitive impairment

A growing body of research suggests that Hispanic ethnicity itself may constitute a risk factor in CI_{mp} [34-36]. Indeed, [37] suggest that Hispanics (like African Americans) may have a greater genetic risk of developing Alzheimer's disease than NHWs; and Mexican Americans may possess a relatively high contingent of risk factors associated with vascular cognitive impairment, including cerebral microvascular disease [22,38,39].

Our findings lend some degree of support to these assertions. After controlling for effects of all other variables in the equation (Blocks 3 of Subtable 1A, Subtable 1B, and Subtable 1C) El Paso's elderly Mexican Americans possess odds 2.46 times greater than NHWs for MMSE impairment, 1.53 times greater for impairment in executive function (CLOXI), and 2.35 times greater for CLOXII impairment. Again, these findings may be clinically relevant to medical professionals whose practices involve routine physical examinations for adult Mexican-American patients.

Importance of using multiple measures of cognitive function

Finally, results in this study point to the importance of utilizing a number of different screening devices for assessment of cognitive function. The author of the CLOX drawing tests [40] suggests that CLOXI is more sensitive to executive function and to dementia presentations similar to those found in Alzheimer's disease than are other clock drawing tests. The CLOX drawing tests are also less sensitive than the MMSE to combined effects of education, SES, acculturation, language, and gender [27], and more able than the MMSE to discover the mild cognitive impairment syndromes found in non-Alzheimer's type dementias [41]. Thus, similar and significant results across multiple measures of cognitive function can discriminate among a variety of dementia-like presentations and increase the likelihood that these results can be taken as valid, dependable, and clinically meaningful.

This is the first study to evaluate the relationships between diabetes, Parkinsonism, and cognitive impairment in the context of Hispanic vs. Non-Hispanic ethnicity.

Funding

This study is supported by grants from the Paso del Norte Foundation's Center for Border Health Research, the United States Department of Health and Human Services Administration on Aging, and the Hogg Foundation for Mental Health.

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